New research could advance research field critical to personalized medicine

December 29 2009

It's the ultimate goal in the treatment of cancer: tailoring a person's therapy based on his or her genetic makeup. While a lofty goal, scientists are steadily moving forward, rapidly exploiting new technologies. Researchers at Georgetown Lombardi Comprehensive Cancer Center report a significant advance in this field of research using a new chip that looks for hundreds of mutations in dozen of genes.

The goal of personalized medicine is to determine the best treatment and the optimal dose carrying the fewest side-effect, especially as new drugs are discovered and treatment options increase. Variations in our genes encode proteins, which impact how a drug is metabolized or taken in by the cells. This directly impacts the drug's effectiveness and the kinds of side-effects that may be caused by its toxicity.

"Currently, available genotyping tools test only a few genes at a time," explains John F. Deeken, a pharmacogentic researcher at Lombardi. "With a new chip called DMET, as many as 170 genes can be examined for more than a thousand variations. This type of turn-key testing, if validated, could eventually replace highly-specialized, time-consuming and labor-intensive testing -- thus allowing more institutes the opportunity to pursue genotyping and pharmocogenetic research. That alone would be a significant development for our field and for expediting the research many of us believe is the future of medicine."

Such a development is particularly critical for cancer research, both in terms of drug discovery and treatment. Genetic variability among

patients in cancer clinical trials is not commonly taken into account, a factor that could skew dosage amounts and doom an otherwise promising new drug. A more simple and faster test could be readily incorporated into treatment trials.

In his paper published online today in *The Pharmacogenomics Journal*, Deeken and colleagues report results of the new genotyping platform called DMET, or drug-metabolizing enzymes and transporters, (Affymetrix, Inc., Santa Clara, Calif.). The DMET "casts a wider net," screening for 1256 genetic variations in 170 genes involved in drug absorption, distribution, metabolism and excretion.

Deeken says one of the main obstacles facing pharmocogenetic researchers like himself is the lack of a proven and relatively quick technology for genotyping. "DMET appears to offer great promise in this field as a reliable test unveiling genetic variations that correlated with drug effectiveness and toxicity," says Deeken. "Still, DMET isn't yet ready for primetime in terms of having received FDA approval, but we're getting closer."

Deeken serves as a consultant to Sanofi-Aventis, the manufacturer of docetaxel, a drug involved in the current reported study. Three other authors are employees of Affymetrix, the manufacturer of the DMET platform. The study was done in part at the National Cancer Institute and supported by funding from the National Institutes of Health.

Provided by Georgetown University Medical Center